the claims in the same application. It is respectfully submitted that in this instance, there is no burden on the Office, because a search should not be required. This application is a continuation-in-part of U.S. application Serial No. 08/695,191, filed August 7, 1996, now U.S. Patent No. 6,025,155, to GYULA HADLACZKY and ALADAR SZALAY, entitled *ARTIFICIAL CHROMOSOMES, USES THEREOF AND METHODS FOR PREPARING ARTIFICIAL CHROMOSOMES*. This application is also continuation-in-part of U.S. application Serial No. 08/682,080, filed July 15, 1996, now U.S. Patent No. 6,077,697, to GYULA HADLACZKY and ALADAR SZALAY, entitled *ARTIFICIAL CHROMOSOMES, USES THEREOF AND METHODS FOR PREPARING ARTIFICIAL CHROMOSOMES*, which is a continuation-in-part of U.S. application Serial No. 08/629,822, filed April 10, 1996.

Restriction requirements were imposed in the parent applications and divisional applications in reliance thereon have been filed. In each of these divisionals further restriction requirements are being imposed, and then in each of the divisionals of the divisionals further restrictions requirements have been imposed. Presently, more than **ten** divisionals have been filed. Yet all of the claims are novel and unobvious because SATACs are novel and unobvious.

As noted, previously, a review of the specification should reveal that the instant claims find basis in the parent applications, which have issued. The claims in the issued patents include claims directed to SATACs per se and to cells containing the SATACs and methods for producing gene products by introducing SATACs into cells. These claims are presumptively novel, unobvious and enabled.

Since SATACs, cells containing SATACS and methods for producing gene products by introducing SATACS into cells, are presumptively novel, unobvious and enabled, claims and methods involving the introduction of SATACs into cells, claims methods using the SATACs must be novel and unobvious, since the SATACs, methods for producing gene produces and cells containing

SATACS are novel and unobvious. The method claims in this case could have been rejoined in one of the parent applications. In addition, since claims involving the introduction of SATACs into cells and to cells containing SATACs have issued, claim 1 in this application must be novel and unobvious and enabled and therefore patentable. Therefore, since no searching or minimal searching is in fact required, there can be no burden on the Office to examine all claims in this application.

As noted in the previous response, if the claims are divided as required by the Examiner, it will never be possible to get a generic claim such as claim 1 examined or issued, despite the fact that similar claims have issued in a parent case. There are no reasons of record to establish that claim 1 should not be issued, particularly, since as noted above, it is presumptively novel, unobvious and enabled.

With respect to requirement for restriction as between groups I and II, and as between III and IV and also as between groups I-IV, the Examiner urges that the materials used by each of the methods differ in structure and function i.e., transformation sequences, and as such, further provides that plant SATACs that are used in animal cells must be changed to allow for expression in a plant cell. It is respectfully submitted that this statement is without basis and is incorrect. A SATAC is a satellite DNA-based artificial chromosome (SATAC)" contain neutral non-coding sequences (heterochromatin) except for foreign heterologous, typically gene-encoding nucleic acid, that is interspersed within the heterochromatin for the expression therein. The delineating structural feature is the presence of repeating units, that are generally predominantly heterochromatin. The precise structure of the depends upon the structure of the chromosome in which the initial amplification event occurs; all share the common feature of including a defined pattern of repeating units and contain more heterochromatin than euchromatin. Foreign nucleic acid molecules (heterologous genes) contained in these artificial chromosome expression

systems can include any nucleic acid whose expression is of interest in a particular host cell. There are no special transformation sequences included in the SATACs; a plant SATAC is one in which the originating chromosome is a plant chromosome; an animal SATAC is one in which the originating chromosome is an animal cell. The heterologous DNA, which includes the regulatory sequences can be any nucleic acid molecules. There is nothing of record that establishes that introduction of a plant SATAC into an animal cell or introduction of an animal SATAC into a plant cell are distinct processes.

Similarly, there is no evidence of record nor any basis to conclude that a plant SATAC functions any differently from an animal SATAC. If required, applicant can provided a DECLARATION under 35 U.S.C. §132 to demonstrate the introduction of a mammalian SATAC into a plant cell (*i.e.*,. claim 8) using substantially the same methods used to introduce a mammalian SATAC into an animal cell. If the requirement is made final Applicant reserves the right to provide such evidence. At this point, however, the burden is on the Office to support the statements made in the restriction requirement.

MPEP 2144.03 states:

> The Examiner may take official notice of facts outside of the record which are capable of instant and unquestionable demonstration as being "well-known" in the art. In re Ahlert, 424 F.2d 1088, 1091, 165 USPQ 418, 420 (CCPA 1970). . . ..

The properties on which the Examiner is basing the requirement for restriction are not "capable of instant and unquestionable demonstration as being "well-known" in the art. The Examiner has not cited any art that demonstrates that plant and animal SATACs function differently or that different methods are needed to produce plant and animal cells containing plant or animal SATACs.

MPEP 2144.03 continues:

> If justified, the examiner should not be obliged to spend time to produce documentary proof. If the knowledge is of such notorious character that official notice can be taken, it is sufficient so to state. In re Malcolm, 129

> F.2d 529, 54 USPQ 235 (CCPA 1942). If the applicant traverses such an assertion the examiner should cite a reference in support of his or her position.

In this instance, there is no evidence that knowledge about the properties of SATACS are of such notorious character that official notice can be taken. Furthermore, since this application in fact is directed to the invention of SATACs, anything related to it must be an esoteric nature. For esoteric technology, MPEP 2144.03 states:

> ("[A]ssertions of technical facts in areas of esoteric technology must always be supported by citation of some reference work" and "allegations concerning specific 'knowledge' of the prior art, which might be peculiar to a particular art should also be supported." Furthermore the applicant must be given the opportunity to challenge the correctness of such assertions and allegations. "**The facts so noticed serve to 'fill the gaps' which might exist in the evidentiary showing" and should not comprise the principle evidence upon which a rejection is based.**). See also In re Barr, 444 F.2d 588, 170 USPQ 330 (CCPA 1971) (scientific journal references were not used as a basis for taking judicial notice that controverted phrases were art-recognized because the court was not sure that the meaning of the term at issue was indisputable among reasonable men); and In re Eynde, 480 F.2d 1364, 1370, 178 USPQ 470, 474 (CCPA 1973) ("The facts constituting the state of the art are normally subject to the possibility of rational disagreement among reasonable men and are not amenable to the taking of [judicial] notice.").

In this instance, the Examiner taking judicial notice provides the crux of the requirement for restriction.

Granted, the methods for introducing nucleic acid into plant cells and animal cells differ somewhat because plant cells have a cell wall. But methods for removing the cell wall to produce protoplasts are well known, and methods introducing nucleic acids into plant and animal cells are well known and are described in the application. The "invention" of the instant application is not the particulars of introducing nucleic acid into particular cells, but in the production of the SATACs. As noted, claims to SATACS and cells per se that contain SATACS have issued in parent applications; this is a divisional application of the issued cases.

Therefore, the restriction requirement should be withdrawn. Furthermore, as presently drafted, there is no way to get claim 1 issued. Thus, at most, the requirement should be recast as an election of species to provide a means to obtain allowance of the generic claim as filed.

* * *

In view of the above amendments and remarks, examination and allowance of the application are respectfully requested.

Respectfully submitted,
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